WEST Search History

DATE: Monday, June 16, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L23	(37 adj kda) same (EGFR or "epidermal growth factor receptor" or HER1)	2	L23
DB=USPT,PGPB,JPAB,EPAB; PLUR=YES; OP=OR			
L22	l17 and (epidermal adj growth adj factor adj receptor)	24	L22
L21	l17 and (epidermal adj growth adj factor)	59	L21
L20	l17 and ab4	0	L20
L19	L17 and (EGFR)	6	L19
L18	L17 and (EGFR or HER1 or epidermal or AB4)	77	L18
L17	37 adj kda	447	L17
DB=DWPI; PLUR=YES; OP=OR			
L16	L15 and (EGFR or epidermal)	1	L16
L15	37 adj kda	15	L15
L14	37 same epidermal	31	L14
L13	37 adj EGFR	0	L13
L12	37	522851	L12
L11	"37kda"	0	L11
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L10	L9 and (HER1 or EGFR or "epidermal growth factor")	2	L10
L9	(Mckeown-S$ or ritchie-j$).in.	164	L9
L8	L7 and (EGFR or epidermal)	78	L8
L7	(37 adj kda)	462	L7
L6	L5 and (EGFR or HER1 or epidermal)	5	L6
L5	37KDa	14	L5
L4	l1 and (EGFR or HER1)	4	L4
L3	Ab4 same EGFR	2	L3
L2	L1 and Oncogene	8	L2
L1	Ab4	269	L1

END OF SEARCH HISTORY

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Welcome to STN International! Enter x:x

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data

```
 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 15:12:53 ON 16 JUN 2003

=> file .gary
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:12:59 ON 16 JUN 2003

FILE 'CANCERLIT' ENTERED AT 15:12:59 ON 16 JUN 2003

FILE 'BIOSIS' ENTERED AT 15:12:59 ON 16 JUN 2003
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FILE 'EMBASE' ENTERED AT 15:12:59 ON 16 JUN 2003
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FILE 'SCISEARCH' ENTERED AT 15:12:59 ON 16 JUN 2003
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=> s (bladder or urinary) and (?carcinoma or cancer? or neoplas? or tumor? or
metast? or carcinoma)
   2 FILES SEARCHED...
   4 FILES SEARCHED...
L1      225999 (BLADDER OR URINARY) AND (?CARCINOMA OR CANCER? OR NEOPLAS? OR
               TUMOR? OR METAST? OR CARCINOMA)

=> s l1 and (EGFR or "epidermal growth factor receptor")
   3 FILES SEARCHED...
L2        1200 L1 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

=> s l2 and "37KDa"
L3           0 L2 AND "37KDA"

=> s l2 and 37kda
L4           0 L2 AND 37KDA

=> s l2 and fragment
L5          30 L2 AND FRAGMENT

=> s McKeown-S?/au or Ritchie-J?/au
L6        3901 MCKEOWN-S?/AU OR RITCHIE-J?/AU

=> s l6 and l2
```

L7 4 L6 AND L2

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 4 DUP REM L7 (0 DUPLICATES REMOVED)

=> d ibib abs 1-4

L8 ANSWER 1 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002275757 EMBASE
TITLE: Prognostic role of P27(kip1) and **epidermal growth factor receptor** in transitional cell **carcinoma** of the **bladder.**
AUTHOR: Valentine A.; **Ritchie J.L.**; Nevin G.B.; **McKeown S.R.**
CORPORATE SOURCE: S.R. McKeown, School of Biomedical Sciences, University of Ulster, County Antrim, Jordanstown BT37 OQB, Ireland. sr.mckeown@ulst.ac.uk
SOURCE: UroOncology, (2002) 2/1 (41-46).
Refs: 26
ISSN: 1561-0950 CODEN: UROOFG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: Presently, there is no reliable method that allows accurate prediction of the clinical course of an individual superficial **bladder** tumour. As 10-20% of superficial **bladder** tumours will become invasive, the discovery of a single or combination of prognostic markers would allow the early establishment of appropriate treatment regimens that could potentially prolong patient life. The aim of this study was to evaluate the potential of both p27 and **epidermal growth factor receptor** (**EGFR**), individually and in combination as prognostic markers for **bladder cancer.** Patients and methods: Immunohistochemistry was used to assess **bladder** tumours for p27 (54 samples), nuclear **EGFR** (65 samples) and 49 biopsies for both markers. Results: To assess p27 expression, a cut-off value of 30% was employed. Associations were found between p27 status and grade, stage, disease recurrence and progression (p = 0.0113, 0.0001, 0.0167 and 0.0024, respectively). Patients presenting with p27 positive tumours had longer disease-free and progression-free survival, compared to p27 negative patients. Through multivariate analysis, p27 was found to be both an independent marker of both recurrence and disease progression (p = 0.0272 and 0.0140, respectively). To assess nuclear **EGFR** expression, a cut-off value of 5% was employed. Associations were found between nuclear **EGFR** expression and disease progression (p = 0.0021) and progression-free survival (log-rank analysis: p= 0.0117). However, when p27 and nuclear **EGFR** expression were combined this provided a superior prognostic indicator than either p27 or nuclear **EGFR** expression alone (univariate p = 0.0013, multivariate: p = 0.008). Conclusions: Individually, both p27 and **EGFR** are excellent predictors of disease progression in **bladder cancer** patients, however when both markers are combined a superior prognostic marker is created. In the future combined p27/**EGFR** staining may lead to the implementation of earlier and more aggressive treatment for patients with a poor prognosis, leading to an improved control of tumours.

L8 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:518427 BIOSIS

DOCUMENT NUMBER: PREV200100518427
TITLE: Predicting progression and survival in **bladder cancer**: Use of p27Kip1 (p27) and **epidermal growth factor receptor** (**EGFR.**
AUTHOR(S): Valentine, A. (1); **Ritchie, J. L. (1)**; Nevin, G. B. (1); **McKeown, S. R. (1)**
CORPORATE SOURCE: (1) School of Biomedical Sciences, University of Ulster, Jordanstown UK
SOURCE: British Journal of Cancer, (July, 2001) Vol. 85, No. Supplement 1, pp. 52. print.
Meeting Info.: Meeting of the British Journal of Cancer Research Leeds, UK July 01-04, 2001
ISSN: 0007-0920.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 2001:679321 SCISEARCH
THE GENUINE ARTICLE: 456CH
TITLE: Predicting progression and survival in **bladder cancer**: Use of p27(kip1) (p27) and **Epidermal Growth Factor Receptor** (**EGFR**)
AUTHOR: Valentine A (Reprint); **Ritchie J L**; Nevin G B; **McKeown S R**
CORPORATE SOURCE: Univ Ulster, Sch Biomed Sci, Jordanstown, North Ireland
COUNTRY OF AUTHOR: North Ireland
SOURCE: BRITISH JOURNAL OF CANCER, (JUL 2001) Vol. 85, Supp. [1], pp. 52-52.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 0007-0920.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

L8 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1998:500426 SCISEARCH
THE GENUINE ARTICLE: ZV718
TITLE: Does a correlation exist between **urinary** EGF, pH and tumour **EGFR** status in **bladder cancer** patients
AUTHOR: **Ritchie J L (Reprint)**; Nevin G B; **McKeown S R**; Johnston S R; Walsh I K
CORPORATE SOURCE: UNIV ULSTER, SCH BIOMED SCI, COLERAINE BT37 0QB, LONDONDERRY, NORTH IRELAND; BELFAST CITY HOSP, DEPT UROL, BELFAST BT9 7AD, ANTRIM, NORTH IRELAND
COUNTRY OF AUTHOR: NORTH IRELAND
SOURCE: BRITISH JOURNAL OF CANCER, (MAY 1998) Vol. 78, Supp. [1], pp. P118-P118.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 0007-0920.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 4

=> d his

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     (FILE 'HOME' ENTERED AT 15:12:53 ON 16 JUN 2003)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 15:12:59
    ON 16 JUN 2003
L1        225999 S (BLADDER OR URINARY) AND (?CARCINOMA OR CANCER? OR NEOPLAS? O
L2          1200 S L1 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")
L3             0 S L2 AND "37KDA"
L4             0 S L2 AND 37KDA
L5            30 S L2 AND FRAGMENT
L6          3901 S MCKEOWN-S?/AU OR RITCHIE-J?/AU
L7             4 S L6 AND L2
L8             4 DUP REM L7 (0 DUPLICATES REMOVED)

=> s l2 and py<=1999
   2 FILES SEARCHED...
   3 FILES SEARCHED...
L9           851 L2 AND PY<=1999

=> s Ab4
L10          252 AB4

=> s l10 and l2
L11            0 L10 AND L2

=> s l10 and l1
L12            0 L10 AND L1

=> d his

     (FILE 'HOME' ENTERED AT 15:12:53 ON 16 JUN 2003)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 15:12:59
     ON 16 JUN 2003
L1        225999 S (BLADDER OR URINARY) AND (?CARCINOMA OR CANCER? OR NEOPLAS? O
L2          1200 S L1 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")
L3             0 S L2 AND "37KDA"
L4             0 S L2 AND 37KDA
L5            30 S L2 AND FRAGMENT
L6          3901 S MCKEOWN-S?/AU OR RITCHIE-J?/AU
L7             4 S L6 AND L2
L8             4 DUP REM L7 (0 DUPLICATES REMOVED)
L9           851 S L2 AND PY<=1999
L10          252 S AB4
L11            0 S L10 AND L2
L12            0 S L10 AND L1

=> dup rem l9
PROCESSING COMPLETED FOR L9
L13          389 DUP REM L9 (462 DUPLICATES REMOVED)

=> s 37kda and (EGFR or "epidermal growth factor receptor)
MISMATCHED QUOTE 'OR "EPIDERMAL'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> s 37kda and (EGFR or "epidermal growth factor receptor")
   3 FILES SEARCHED...
L14            0 37KDA AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

=> file pctfull
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY     SESSION
FULL ESTIMATED COST                            36.48      36.69
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FILE 'PCTFULL' ENTERED AT 15:29:27 ON 16 JUN 2003
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FILE LAST UPDATED:         10 JUN 2003      <20030610/UP>
MOST RECENT UPDATE WEEK:       200322        <200322/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s 37kda
L15          42 37KDA

=> s l15 and (EGFR or "epidermal growth factor receptor")
           1391 EGFR
             33 EGFRS
           1392 EGFR
                  (EGFR OR EGFRS)
          11241 "EPIDERMAL"
              8 "EPIDERMALS"
          11247 "EPIDERMAL"
                  ("EPIDERMAL" OR "EPIDERMALS")
          91266 "GROWTH"
           1509 "GROWTHS"
          91578 "GROWTH"
                  ("GROWTH" OR "GROWTHS")
         115350 "FACTOR"
         119062 "FACTORS"
         173138 "FACTOR"
                  ("FACTOR" OR "FACTORS")
          49969 "RECEPTOR"
          37337 "RECEPTORS"
          55974 "RECEPTOR"
                  ("RECEPTOR" OR "RECEPTORS")
           1492 "EPIDERMAL GROWTH FACTOR RECEPTOR"
                  ("EPIDERMAL"(W)"GROWTH"(W)"FACTOR"(W)"RECEPTOR")
L16            3 L15 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

=> d ibib abs kwic 1-3

L16    ANSWER 1 OF 3     PCTFULL   COPYRIGHT 2003 Univentio
ACCESSION NUMBER:        2002040710 PCTFULL  ED 20020610  EW 200221
TITLE (ENGLISH):         METHOD FOR DETECTING METHYLATION STATES FOR A
                         TOXICOLOGICAL DIAGNOSTIC
TITLE (FRENCH):          PROCEDE DE DETECTION D'ETATS DE METHYLATION AFIN DE
                         PERMETTRE LE DIAGNOSTIC TOXICOLOGIQUE
TITLE (GERMAN):          VERFAHREN ZUR DETEKTION VON METHYLIERUNGSZUSTAeNDEN ZUR
                         TOXIKOLOGISCHEN DIAGNOSTIK
INVENTOR(S):             OLEK, Alexander, Schroederstrasse 13, 10115 Berlin, DE
                         [DE, DE];
                         PIEPENBROCK, Christian, Schwartzkopffstrasse 7 B, 10115
                         Berlin, DE [DE, DE];
                         BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahnsdorf, DE
                         [DE, DE]
PATENT ASSIGNEE(S):      EPIGENOMICS AG, Kastanienallee 24, 10435 Berlin, DE
                         [DE, DE], for all designates States except US;
                         OLEK, Alexander, Schroederstrasse 13, 10115 Berlin, DE
                         [DE, DE], for US only;
                         PIEPENBROCK, Christian, Schwartzkopffstrasse 7 B, 10115
                         Berlin, DE [DE, DE], for US only;
                         BERLIN, Kurt, Marienkaeferweg 4, 14532 Stahnsdorf, DE
                         [DE, DE], for US only
AGENT:                   SCHUBERT, Klemens, Neue Promenade 5, 10178
                         Berlin-Mitte, DE
LANGUAGE OF FILING:      German
LANGUAGE OF PUBL.:       German
```

DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2002040710	A2	20020523

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-EP12951 A 20011108

PRIORITY INFO.: DE 2000-100 56 802.5 20001114

ABEN The invention relates to a method for a toxicological diagnostic. According to the invention, a DNA sample is taken from an organism or a cell culture which has been exposed to a specific substance which is to be examined on account of its toxicological effect. The DNA contained in said sample is chemically pre-treated and the base sequence of a section of the modified DNA is determined. From there, a characteristic methylation state or a characteristic methylation model is determined for the sample. By comparison with data from methylation states of other samples, the effect of a substance on the organism or the cell culture is determined and/or compared to other substances in toxicological terms.

ABFR La presente invention concerne un procede permettant le diagnostic toxicologique. Un echantillon d'ADN est preleve chez un etre vivant ou une culture cellulaire qui a ete prealablement expose a une substance donnee a activite toxicologique a analyser. L'ADN contenu dans cet echantillon est pretraite chimiquement et la sequence de bases d'une partie de l'ADN modifie est determinee. A partir de cela, un etat de methylation caracteristique de l'echantillon ou un motif de methylation caracteristique est determine. Grace a la comparaison avec des donnees relatives a des etats de methylation d'autres echantillons, l'activite d'une substance sur l'etre vivant ou sur la culture cellulaire est determinee et/ou comparee avec celle d'autres substances d'un point de vue toxicologique.

ABDE Die vorliegende Erfindung betrifft ein Verfahren zur toxikologischen Diagnostik. Einem Lebewesen oder einer Zellkultur, die zuvor einer bestimmten auf ihre toxikologische Wirkung zu untersuchende Substanz ausgesetzt wurden, wird eine DNA-Probe entnommen. Die in dieser Probe enthaltene DNA wird chemisch vorbehandelt und die Basenabfolge eines Teils der modifizierten DNA bestimmt. Daraus wird auf einen fuer die Probe charakteristischen Methylierungszustand oder ein charakteristisches Methylierungsmuster geschlossen. Durch den Abgleich mit Daten aus Methylierungszustaenden anderer Proben wird auf die Einwirkung einer Substanz auf das Lebewesen oder

die Zellkultur geschlossen und/oder mit anderen Substanzen in toxikologischer
Hinsicht verglichen.

DETD . . . kDa-Untereinheit (RFC36);
Aktivator 36-kDa-Untereinheit LO7540
Replikationsfaktor-C kDa-Untereinheit (RFC38);
Aktivator 38-kDa-Untereinheit LO7541
Replikations-Protein-A kDa-Untereinheit
(RPA70; REPA1; RF-A); einzelstraengige-DNA-bindendes
Protein M63488
Aktivator 40-kDa-Untereinheit (A1 kDa-
Untereinheit); Replikationsfaktor-C-40kDa-
Untereinheit (RFC40); RFC2 M87338
Aktivator **37kDa**-Untereinheit; Replikationsfaktor-
C-**37kDa**-Untereinheit (RFC37); RFC4 M87339
DNA-Topoisomerase I (TOP1) J03250
DNA-Topoisomerase II alpha (TOP2A) J04088
proliferierendes zyklisches Kern-Antigen (PCNA);

In Figur 3 ist der Methylierungsstatus ausgewaehlter CpGs
fuer die Gene TGF-a. **EGFR**, ANT1 und E-Cadherin quantitativ
ERSATZBLATT (REGEL 26)
dargestellt. Die Amplifikation dieser Genen erfolgte unter den in Beispiel 2 beschrieben Bedingungen. In Tabelle 2. . . u. 2, D1). In einem weiteren
Experiment wurde der Einfluss von Milrinon und Trichostatin auf den Methylierungsstatus ausgewaehlter CpG-Positionen der Gene **EGFR**, ANT1 und CDC25A untersucht. Die Behandlung der HT29-P208 Zellen mit Milrinon fuehrte zu einer Verringerung, mit Trichostatin zu einer Erhoehung des Methylierungsstatus (siehe. . .
. . .
repraesen-
tiert werden, wurden aus folgenden Genen untersucht: TGF-a (A1, oligo SEQ IDs 6, 7; A2, oligo SEQ IDs 8f 9)f **EGFR** (B1, oligo SEQ IDs 20, 21; B2, oligo SEQ IDs 22, 23), ANT1 (C1, oligo SEQ IDs 321 33; C2, oligo SEQ. . .
. . .
(graue
Saeulen) und Milrinon (weisse Saeulen) behandelten HT29-P208 Zellen. CpGs, die durch die angegebenen Oligo-SEQ IDs repraesentiert werden, wurden aus folgenden Genen untersucht: **EGFR**(A1, oligo SEQ IDs 22, 23)f ANT1 (B1f oligo SEQ IDs 32, 33; B2, oligo SEQ IDs 34, 35) und CDC25A (C1, oligo. . .

CLMDE Aktivator 38-kDa-Untereinheit LO7541
Replikations-Protein-A kDa-Untereinheit
(RPA70; REPA1; RF-A); einzelstraengige-DNA-bindendes Protein M63488
Aktivator 40-kDa-Untereinheit (A1 kDa-
Untereinheit); Replikationsfaktor-C-40kDa-
Untereinheit (RFC40); RFC2 M87338
Aktivator **37kDa**-Untereinheit; Replikations-
faktor-C-**37kDa**-Untereinheit (RFC37); RFC4 M87339
DNA-Topoisomerase I (TOP1) J03250
DNA-Topoisomerase II alpha (TOP2A) J04088
proliferierendes zyklisches Kern-Antigen
(pcNA); zyklin M15796; J04718
DNA-Topoisomerase II beta (TOP2B) X68060
Replikations-Protein-A-14kDa-Untereinheit
RP-A) (RF-A);. . .

L16 ANSWER 2 OF 3 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 2002034771 PCTFULL ED 20020515 EW 200218

TITLE (ENGLISH): NUCLEIC ACIDS AND PROTEINS FROM STREPTOCOCCUS GROUPS A & B

TITLE (FRENCH): ACIDES NUCLEIQUES ET PROTEINES DERIVES DES GROUPES DE STREPTOCOQUES A ET B

INVENTOR(S): TELFORD, John, Chiron S.p.a, Via Fiorentina, 1, I-53100 Siena, IT [GB, IT];
MASIGNANI, Vega, Chiron S.p.a, Via Fiorentina, 1, I-53100 Siena, IT [IT, IT];
MARGARIT Y ROS, Immaculada, Chiron S.p.a, Via Fiorentina, 1, I-53100 Siena, IT [IT, IT];
GRANDI, Guido, Chiron S.p.a, Via Fiorentina, 1, I-53100 Siena, IT [IT, IT];
FRASER, CLAIRE, The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850, US [US, US];
TETTELIN, Herve, The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850, US [BE, US]

PATENT ASSIGNEE(S): CHIRON S.P.A., Via Fiorentina, 1, I-53100 Siena, IT [IT, IT], for all designates States except US;
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MASIGNANI, Vega, Chiron S.p.a, Via Fiorentina, 1, I-53100 Siena, IT [IT, IT], for US only;
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LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002034771	A2	20020502

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-GB4789 A 20011029
PRIORITY INFO.: GB 2000-0026333.5 20001027
GB 2000-0028727.6 20001124
GB 2001-0105640.7 20010307

ABEN The invention provides proteins from group B streptococcus (Streptococcus agalactiae) and group A streptococcus (Streptococcus pyogenes), including amino acid sequences and the

corresponding nucleotide sequences. Data are given to show that the proteins are useful antigens for vaccines, immunogenic compositions, and/or diagnostics. The proteins are also targets for antibiotics.

ABFR Cette invention se rapporte a des proteines derivees du streptocoque de groupe B (Streptococcus agalactiae) et du streptocoque de groupe A (Streptococcus pyogenes), y compris des sequences d'acides amines et les sequences de nucleotides correspondantes. On produit des donnees qui montrent que ces proteines constituent des antigenes utiles pour des vaccins, des compositions immunogenes et/ou des diagnostics. Ces proteines constituent egalement des cibles pour des antibiotiques.

DETD data too large for display

DETD data too large for display

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DETD data too large for display

DETD data too large for display

DETD data too large for display

L16 ANSWER 3 OF 3 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 2000019208 PCTFULL ED 20020515

TITLE (ENGLISH): **EGFR** 37 KDA FRAGMENT AS CANCER MARKER

TITLE (FRENCH): FRAGMENT DE 37 KDA D'**EGFR** (RECEPTEUR DU FACTEUR DE CROISSANCE EPIDERMIQUE) UTILE COMME MARQUEUR DE CANCER

INVENTOR(S): McKEOWN, Stephanie;
RITCHIE, Joan

PATENT ASSIGNEE(S): UNIVERSITY OF ULSTER AT JORDANSTOWN;
McKEOWN, Stephanie;
RITCHIE, Joan

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000019208	A1	20000406

DESIGNATED STATES

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-GB3235 A 19990930

PRIORITY INFO.: GB 1998-9821170.9 19980930

ABEN The present invention relates to the presence of a **37KDa epidermal growth factor receptor** (**EGFR**) fragment in the urine of patients with transitional cell carcinoma of the bladder. The presence of the **37KDa EGFR** fragment in urine can be ascertained using an antibody. The presence of the **37KDa EGFR** fragment in the urine of patients can be a test for the presence of prostate cancer and can therefore be used as a general screen for health in the genitourinary area.

ABFR L'invention a trait a la presence d'un fragment d'**EGFR** de 37 KDa dans l'urine de patients presentant un carcinome transitionnel de la vessie. La presence du fragment d'**EGFR** de **37KDa** dans l'urine peut etre determinee au moyen d'un anticorps. La presence du fragment d'**EGFR** de **37KDa** dans l'urine de patients peut constituer un test de la presence d'un cancer de la prostate, et peut par consequent etre utilise comme test general de depistage de la zone genito-urinaire.

TIEN **EGFR** 37 KDA FRAGMENT AS CANCER MARKER

TIFR FRAGMENT DE 37 KDA D'**EGFR** (RECEPTEUR DU FACTEUR DE CROISSANCE EPIDERMIQUE) UTILE COMME MARQUEUR DE CANCER

ABEN The present invention relates to the presence of a **37KDa epidermal growth factor receptor** (**EGFR**) fragment in the urine of patients with transitional cell carcinoma of the bladder. The presence of the **37KDa EGFR** fragment in urine can be ascertained using an antibody. The presence of the **37KDa EGFR** fragment in the urine of patients can be a test for the presence of prostate cancer and can therefore be. . .

ABFR L'invention a trait a la presence d'un fragment d'**EGFR** de 37 KDa dans l'urine de patients presentant un carcinome transitionnel de la vessie. La presence du fragment d'**EGFR** de **37KDa** dans l'urine peut etre determinee au moyen d'un anticorps. La presence du fragment d'**EGFR** de **37KDa** dans l'urine de patients peut constituer un test de la presence d'un cancer de la prostate, et peut par consequent. . .

DETD **EGFR** 37 KDA FRAGMENT AS CANCER MARKER

3 The present invention relates to a method of diagnosis of bladder cancer or prostate cancer. . .

is

The invention relates to the presence of a **37KDa epidermal growth factor receptor** (**EGFR**) fragment in the urine of patients with transitional cell carcinoma of the bladder (TCCB) and in the urine of some patients with prostate. . .

26 The **37KDa** fragment can be observed in a western blot of proteins from a urine sample from a patient with TCCB.

29 According to the present invention there is provided a marker for bladder cancer, the marker comprising a **37KDa EGFR** fragment which is detectable in urine.

36 The invention provides a test for the presence of a **37KDa EGFR** fragment in urine, the test comprising detecting the **37KDa EGFR** fragment with an antibody.

. . .

these, the method comprising the steps of reacting a urine sample from an individual to be tested with means to detect a **37KDa EGFR** fragment and analysing results.

19 In one embodiment the means to detect the **37KDa EGFR** fragment is an antibody.

22 Preferably the antibody is raised against a peptide

corresponding to amino acid residues 1005 to 1016 of **EGFR** or binds to such a peptide or a peptide substantially similar thereto.

27 A substantially similar peptide is 60% homologous to the amino acid sequence along at least 50% of the length of the **37KDa** peptide.

31 In a particular embodiment of the invention the antibody is Ab4 **EGFR** antibody available from Oncogene Science, Inc.

35 The invention further provides the use of antibody Ab4 **EGFR** in a test to detect the present of 34KDa **EGFR** fragment in urine.

3 The invention also encompasses the use of specific antibodies raised to the **37KDa** fragment of **EGFR.**

Experiment 1
is A **37KDa EGFR** fragment has been detected in urine from
patients with bladder cancer. First morning urine samples were collected from 24 TCC patients, 6. . . 1100C for 20 minutes, all samples were stored at -
700C until required for analysis. Samples were then probed with the Ab4 **EGFR** antibody (Oncogene Sciences) to the internal domain of the receptor by western blot analysis.

Disease Status	No	Presence of the **37KDA** Fragment	Absence of the **37KDA** Fragment
Healthy	13	1	12
TCC	24	21	3
Remission (disease free)	6	4	2

A **37KDa** fragment was detected in 88% (21/24) of TCC patients, 66% (4/6) of disease free patients and 7% (1/13) of healthy volunteer urine samples. There was an overall significant association-between detection of the **37KDa** fragment and presence of bladder cancer.

tested positively, two had frank low grade tumours and two had bladder inflammation at the time the urine sample was taken. This **37KDa** fragment - therefore appears to be of diagnostic importance. it has a much higher sensitivity than urinary cytology and the Bard BTA and. . .

Experiment 2

Disease Status	Numbert	Presence of the **37KDA** Fragment	Absence of the **37KDA** Fragment	(CHI)2
Healthy	25(13)	1(4%)	24(96%)	
Urinary Infection	16(12)	10(62.5%)	6(37.5%)	
Remission (disease free)	6(2)t 0	6(100%)		46.17*
TCC	32(24)	28(87.5%)	4(12.5%)	
Prostate Cancer	10(0)	5(50%)	5(50%)	

Sensitivity levels for the detection of a **37KDa EGFR** fragment in urine.

It is possible that the **37KDa** protein could be used to distinguish between stage or grade in prostate cancer.

. . .

patients
tested positive and 37.5% tested negative
50% of the prostate cancer patients test positive
3 to date, the overall sensitivity of the **37KDa**
protein is 87% and the specificity is 96%.

6 statistical analysis shows that detection of the
37KDa fragment is dependent on the presence of
disease (chj2 =46.17 p<0.001).

10 Detection of the 37KDR **EGFR** fragment in urine
12 From the investigations carried out on the detection of
the **37KDa EGFR** fragment, it has been statistically
established that the detection of the protein is
dependent on disease presence. The fact that all
remission patients analysed, tested negative for the
37KDa fragment is very encouraging. To date the
overall sensitivity of the fragment protein is 87% and
the specificity is 96%. Both these. . . and the BTA stat are 48% and
57%
respectively, with specificites of 70% and 68%
respectively (Weiner et al, 1998). However, the **37KDa**
EGFR fragment test is not 100% sensitive or specific.

. . .

did not pick up 4 patients who had bladder
tumours at the time of analysis. It may therefore be
suggested that the **37KDa** test could be used in tandem
with both the NMP22 and the BTA stat test to reach 100%
sensitivity and specificity. If. . .

4 Of the prostate patients analysed, 50% tested positive
for the **37KDa** fragment. The medical records of these
patients will have to be researched further to confirm
if they also had a undetected bladder. . .

13 From the data obtained it was also found that 57% of
urinary infection patients tested positive for the
37KDa fragment. This was to be expected, as **EGFR**
over
expression has been associated with inflammation and
chronic irritation (Uhlman et al., 1996). The urinary
infection patients would have to be treated with a
course of antibiotics before the **37KDa** test could be
carried out. The **37KDa** fragment test has a number of
clinical uses. Firstly, the test could be used to
determine whether or not a patient requires. . .

. . .

Bard TRAK test
while more sensitive has yet to be marketed and in fact
the results from the present study indicate that the
37KDa EGFR fragment is at least comparable. Further
work is required to investigate the significance of
this fragment in the detection of first presentation
and. . .

19 The **37KDa EGFR** fragment may be used as a detector
for
first presentation bladder and recurrent bladder TCC.

Detection of the **37KDa EGFR** fragment may be carried
out

by other methods of investigation as well as western blot analysis. These methods may include immunochromatography, ELISA, latex. . . There is currently available a one-
step immunochromatographic assay which qualitatively detects bladder tumour antigen in urine in five minutes. Detection of the **37KDa EGFR** fragment may be detected by a similar method. Patient urine would be added to the small chamber where it mixes with a colloidal gold-conjugated antibody. If the **37KDa** fragment is present, a **37KDa** fragment conjugate complex would form. The reaction mixture would flow through the membrane which contains zones of immobilised capture antibodies. In the test zone, the **37KDa** fragment conjugate complexes would be capture y a second antigen-specific antibody,-forming a visible line. If the **37KDa** fragment is not present in the urine, no visible line would form.

. . .
Oncogene Science,
Inc. as catalogue no. HCS16. There is no suggestion that the antibody could be used to diagnose the presence of the **37KDa EGFR** fragment in urine or that the presence of this fragment is indicative of bladder or prostate cancer.

Other antibodies can be developed which are specific to the **37KDa** fragment. This may increase sensitivity of the test.

. . .
1986) and health status
(Thrasher et al, 1994). None of these factors can predict prognosis in 100% of patients and so the **37KDa** fragment may have some use prognostically. The **EGFR** fragment may be detected quantitatively using densitometry following western blot analysis and used to predict whether increased levels indicate a better or worse prognosis.. . .

EGF and **EGFR** have been implicated i-n the pathogenesis of solid tumours such as those of the breast. This simple test developed for urine of patients with suspected TCCB might also be used to identify the diagnostic prognostic role of serum **EGFR** in other tumour types.

CLMEN 3 1. A marker for bladder cancer, prostate cancer or urinary infection, the marker comprising a **37KDa** fragment of **EGFR.**

2 A method for the diagnosis of first presentation or recurrence of bladder cancer, the method comprising the detection of a **37KDa** fragment of **EGFR** in a urine sample.

3 A method as claimed in claim 2 wherein the presence of the **37KDa EGFR** fragment is detected using an antibody.

4 A method as claimed in claim 2 or claim 3 wherein the presence of **37KDa EGFR** fragment is detected using antibody Ab4 **EGFR** available from Oncogene Science, Inc.

5 The use of antibody Ab4 **EGFR** in a test to detect

the presence of **37KDa EGFR** fragment in urine as a diagnostic test for bladder cancer.

6 A method for the diagnosis of prostate cancer, the method comprising the detection of a **37KDa** fragment of **EGFR** in a urine sample.

7 A method as claimed in claim 6 wherein the presence of the **37KDa EGFR** fragment is detected using an antibody.

8 A method as claimed in claim 6 or claim 7 wherein the presence of **37KDa EGFR** fragment is detected using antibody Ab4 **EGFR** available from Oncogene Science, Inc.

9 The use of antibody Ab4 **EGFR** in a test to detect the presence of **37KDa EGFR** fragment in urine as a diagnostic test for prostate cancer.
5 10. A method for the diagnosis of bladder cancer, and/or prostate cancer and/or urinary infectiorL, the method comprising a test for the presence of a **37KDa** fragment of **EGFR** in a urine sample.
10 11. A method as claimed in any of claims 2 to 4 and 7 to 10 in. . .

12 The use of antibodies to the **37KDa** fragment of **EGFR** in the diagnosis of urinary infection, bladder cancer and prostate cancer.
18
MTERNATIONAL SEARCH REPORT
Inter snal Application No
PCT/GB 99/03235
A. CLASSIFICATION OF SUBJECT MATTER
IPC. . .

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=> d his

     (FILE 'HOME' ENTERED AT 15:12:53 ON 16 JUN 2003)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 15:12:59
     ON 16 JUN 2003
L1       225999 S (BLADDER OR URINARY) AND (?CARCINOMA OR CANCER? OR NEOPLAS? O
L2         1200 S L1 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")
L3            0 S L2 AND "37KDA"
L4            0 S L2 AND 37KDA
L5           30 S L2 AND FRAGMENT
L6         3901 S MCKEOWN-S?/AU OR RITCHIE-J?/AU
L7            4 S L6 AND L2
L8            4 DUP REM L7 (0 DUPLICATES REMOVED)
L9          851 S L2 AND PY<=1999
L10         252 S AB4
L11           0 S L10 AND L2
L12           0 S L10 AND L1
L13         389 DUP REM L9 (462 DUPLICATES REMOVED)
L14           0 S 37KDA AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

     FILE 'PCTFULL' ENTERED AT 15:29:27 ON 16 JUN 2003
L15          42 S 37KDA
L16           3 S L15 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

=> s l13 and urine
L13 CANNOT BE SEARCHED IN PCTFULL
The L-number cannot be used because it does not contain a query.
```

```
Enter DISPLAY HISTORY to see the sequence of commands that created
this L-number.

=> file .gary
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.84      44.53

FILE 'MEDLINE' ENTERED AT 15:31:57 ON 16 JUN 2003

FILE 'CANCERLIT' ENTERED AT 15:31:57 ON 16 JUN 2003

FILE 'BIOSIS' ENTERED AT 15:31:57 ON 16 JUN 2003
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=> s l13 and urine
L17         25 L13 AND URINE

=> d his

     (FILE 'HOME' ENTERED AT 15:12:53 ON 16 JUN 2003)

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 15:12:59
     ON 16 JUN 2003
L1       225999 S (BLADDER OR URINARY) AND (?CARCINOMA OR CANCER? OR NEOPLAS? O
L2         1200 S L1 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")
L3            0 S L2 AND "37KDA"
L4            0 S L2 AND 37KDA
L5           30 S L2 AND FRAGMENT
L6         3901 S MCKEOWN-S?/AU OR RITCHIE-J?/AU
L7            4 S L6 AND L2
L8            4 DUP REM L7 (0 DUPLICATES REMOVED)
L9          851 S L2 AND PY<=1999
L10         252 S AB4
L11           0 S L10 AND L2
L12           0 S L10 AND L1
L13         389 DUP REM L9 (462 DUPLICATES REMOVED)
L14           0 S 37KDA AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

     FILE 'PCTFULL' ENTERED AT 15:29:27 ON 16 JUN 2003
L15          42 S 37KDA
L16           3 S L15 AND (EGFR OR "EPIDERMAL GROWTH FACTOR RECEPTOR")

     FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 15:31:57
     ON 16 JUN 2003
L17          25 S L13 AND URINE

=> s l13 and antibod?
L18         104 L13 AND ANTIBOD?

=> s l18 and urine
L19           6 L18 AND URINE

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20           6 DUP REM L19 (0 DUPLICATES REMOVED)

=> d ibib abs 1-6
```

L20 ANSWER 1 OF 6 MEDLINE
ACCESSION NUMBER: 1998103968 MEDLINE
DOCUMENT NUMBER: 98103968 PubMed ID: 9443731
TITLE: Technetium-99m-labeled anti-EGF-receptor **antibody** in patients with **tumor** of epithelial origin: I. Biodistribution and dosimetry for radioimmunotherapy.
AUTHOR: Iznaga-Escobar N; Torres L A; Morales A; Ramos M; Alvarez I; Perez N; Fraxedas R; Rodriguez O; Rodriguez N; Perez R; Lage A; Stabin M G
CORPORATE SOURCE: Center of Molecular Immunology, Institute of Nephrology, Orthopedic Hospital Frank Pais, Havana, Cuba.
SOURCE: JOURNAL OF NUCLEAR MEDICINE, **(1998 Jan)** 39 (1) 15-23.
Journal code: 0217410. ISSN: 0161-5505.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 20000303
Entered Medline: 19980213

AB Accurate estimation of biodistribution and absorbed dose to normal organs and **tumors** is important for immunoscintigraphic studies and radioimmunotherapy treatment planning. METHODS: Four patients (3 men, 1 woman; mean age 54.8 +/- 9.2 yr; range 42-64 yr) were administered 3 mg of anti-human **epidermal growth factor receptor** (anti-hEGF-r) **antibody** (ior egf/r3), radiolabeled with 99mTc activity of 39.5 +/- 1.1 mCi (range 38.5 mCi-40.7 mCi) by intravenous bolus infusion. After administration, blood and **urine** samples were collected from three patients up to 24 hr after injection. Whole-body anterior and posterior scans were obtained at 5 min and 1, 3, 5 and 24 hr after injection. Using a computer program, regions of interest were drawn over the heart, liver, spleen, **bladder** and **tumor** to measure the activity in the source organs at each scanning time. Time-activity curves for each source organ were then fitted to monoexponential or biexponential functions by nonlinear least squares regression using the flexible polyhedrals method, which adequately fit our data with the correlation coefficient of 0.985 +/- 0.013, and were integrated to determine organ residence times. The mean absorbed doses to the whole body and various normal organs were then estimated from residence times and from blood and **urine** samples using the methods developed by the Medical Internal Radiation Dose Committee. The effective dose equivalent and effective dose were calculated as prescribed in ICRP Publication Nos. 30 and 60. RESULTS: Plasma disappearance curves of 99mTc-labeled anti-hEGF-r **antibody** were best-fit by a two-compartment model in all patients with a distribution half-life (t(1/2alpha)) of 0.207 hr +/- 0.059 hr (mean +/- s.d., n = 3) and an elimination half-life (t(1/2beta)) of 13.9 hr +/- 2.2 hr. Among the various organs, significant accumulation of the radiolabeled **antibody** was found in the liver (48.5% +/- 4.4%, mean +/- s.d.), heart (3.50% +/- 0.17%) and spleen (3.1% +/- 1.8%) at 5 min postadministration. These values were reduced to 3.2% +/- 0.4%, 0.1% +/- 0.01% and 0.1% +/- 0.1%, respectively, at 24 hr. Mean cumulative **urinary** excretion of 99mTc-labeled anti-hEGF-r **antibody** was 4.6% +/- 0.6% at 24 hr postinjection. Estimates of radiation absorbed dose to normal organs in rad/mCi administered (mean +/- s.d., n = 4) were: whole body 0.017 +/- 0.002; gallbladder wall 0.074 +/- 0.007; spleen 0.136 +/- 0.076; and liver 0.267 +/- 0.036. The effective dose equivalent and effective dose estimates for adults were 0.041 +/- 0.008 rem/mCi and 0.027 +/- 0.004 rem/mCi administered. CONCLUSION: This feasibility study indicates that 99mTc-labeled anti-hEGF-r **antibody** (ior egf/r3) can be used safely; this analysis provides a dosimetric framework for future studies. This monoclonal **antibody**, labeled with 188Re, could possibly permit a successful regional radioimmunotherapy of

tumors of epithelial origin.

L20 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:128090 BIOSIS
DOCUMENT NUMBER: PREV199598142390
TITLE: Biological disposition of intravenously administered 131I-labeled anti-EGF-receptor **antibody** (RG 83852) in the rat.
AUTHOR(S): Khetarpal, V. K. (1); Storbeck, L. S.
CORPORATE SOURCE: (1) Drug Disposition, Rhone-Poulenc Rorer, 500 Arcola Raod, Collegeville, PA 19426 USA
SOURCE: Cancer Chemotherapy and Pharmacology, (1995) Vol. 35, No. 4, pp. 313-317.
ISSN: 0344-5704.
DOCUMENT TYPE: Article
LANGUAGE: English
AB RG 83852 is a murine monoclonal **antibody** that preferentially inhibits the high-affinity binding of epidermal growth factor (EGF) to its receptor. Since overexpression of EGF receptor has been implicated in some human malignancies, the **antibody** is under investigation as a potential anticancer agent. The present work characterized the tissue distribution and elimination of 131I-labeled **antibody** in rats following i. v. administration. 121I-RG 83852 was given in a 2.22 mg/kg dose to rats, and 4, 24, 48, and 72 h afterwards 131I activity excreted in the **urine** and feces and that present in various tissues was determined. The plasma contained the highest concentration of radioactivity at all times. At 4 h the plasma contained about 12% of the injected dose (ID)/ml, and radioactivity in this compartment accounted for almost 70% ID. The plasma elimination of 131I-derived activity occurred linearity at a rate of about 0.48% ID/h. Except in the thyroid, the concentration of 1311 activity in all tissues was much lower than in the plasma (tissue-to-plasma ratio ltoreq 0.1). In the thyroid, accumulation of radioactivity (4% ID at 24 h) was presumably due to trapping of 131I released from the **antibody** as a result of biodegradation. The **urinary** excretion occurred at a rate of about 0.5% ID/h; the fecal excretion was minimal. The biodistribution results are consistent with the protein structure of the **antibody.** Based on the available disposition data, it is proposed that elimination of the **antibody** involves degradation, a process that follows zero-order kinetics, followed by excretion of the labeled product(s) in the **urine.**

L20 ANSWER 3 OF 6 MEDLINE
ACCESSION NUMBER: 95334861 MEDLINE
DOCUMENT NUMBER: 95334861 PubMed ID: 7541921
TITLE: Epithelial differentiation antigens and **epidermal growth factor receptors** in transitional cell **bladder carcinoma**: correlation with prognosis.
AUTHOR: Nakopoulou L; Zervas A; Constantinides C; Deliveliotis C; Stefanaki K; Dimopoulos C
CORPORATE SOURCE: Department of Urology, Athens University Medical School, Greece.
SOURCE: UROLOGIA INTERNATIONALIS, **(1995)** 54 (4) 191-7.
Journal code: 0417373. ISSN: 0042-1138.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 19950828
Last Updated on STN: 20000303
Entered Medline: 19950816
AB Epithelial differentiation antigens have been correlated with morphologic differentiation of **neoplastic** urothelium. Moreover, epidermal growth factor, which is a polypeptide regulating growth and

differentiation of normal and **neoplastic** cells, is found in high concentrations in the **urine** while its receptors (**EGFR**) have been identified in **bladder tumors.** The aim of this study was to investigate the immunohistochemical expression of cytokeratin, epithelial membrane antigen (EMA), CEA and **EGFR** in transitional cell **bladder carcinomas** (TCC) and to define any correlation of their expression with **tumor** grade, stage and patient survival. Twenty-four biopsy specimens obtained from patients with TCC were studied retrospectively. There were 23 men and 1 woman with a mean follow-up of 64 months. Eight biopsy specimens, which represented **tumor** recurrences of 4 patients, were also included in our material. The immunohistochemical avidin-biotin complex method was performed on paraffin sections for the detection of cytokeratin and **EGFR** with monoclonal **antibodies** as well as CEA with a polyclonal **antibody.** Cytokeratin was detected in 83.5% of the TCC, EMA in 62% and CEA in 70%. The expression of the epithelial differentiation antigens in TCCs was heterogenous, showing an increased incidence in high-grade and high-stage TCC. The CEA expression in TCC demonstrated a statistically significant correlation with patient survival ($p < 0.02$). **EGFR** was detected in 50% of the TCC. Although not statistically significant, a trend was found for a higher percentage of **EGFR** detection in high-grade TCC. **EGFR** expression was significantly associated with **tumor** stage and patient survival ($p < 0.01$ and $p < 0.04$, respectively).(ABSTRACT TRUNCATED AT 250 WORDS)

L20 ANSWER 4 OF 6 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 94:588717 SCISEARCH
THE GENUINE ARTICLE: NE169
TITLE: DERANGED ACTIVITY OF THE CD44 GENE AND OTHER LOCI AS BIOMARKERS FOR PROGRESSION TO **METASTATIC** MALIGNANCY
AUTHOR: TARIN D (Reprint); MATSUMURA Y
CORPORATE SOURCE: UNIV OXFORD, JOHN RADCLIFFE HOSP, NUFFIELD DEPT PATHOL, OXFORD OX3 9DU, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (**1993**) Supp. 17G, pp. 173-185.
ISSN: 0730-2312.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB About one in three people in modem industrialised countries die of the consequences of malignant tumours or are found to carry an unsuspected one at the time of autopsy. Early resection of such lesions and appropriate adjuvant therapy is very effective in curing the disease. There is therefore a strong clinical incentive to find effective methods of early diagnosis, assessment of prognosis and treatment of **neoplastic** lesions and research on this topic is directed at a numerically significant medical problem.

Recently it has been found that many human tumours show severe abnormalities in the expression of the CD44 gene which increase with progression to **metastatic** malignancy. By alternative splicing mechanisms this gene codes for a family of heavily glycosylated cell surface proteins involved in many important cellular activities. In **neoplasia** there is gross overexpression of various products of the gene associated with disorderly splicing, which can be detected in clinical samples with the sensitive technique of reverse transcription-polymerase chain reaction (RT-PCR). These disturbances begin early in the **neoplastic** process and can be detected in very small biopsy samples. It has also been shown that it is possible to achieve non-invasive diagnosis of malignancy by analysis of CD44 expression in exfoliated cells in body fluids and waste products. The potential significance of these observations for early diagnosis of

symptomatic **cancer** and for screening of the population for asymptomatic lesions are readily seen and await further investigation.

Separate work in our laboratory has succeeded in DNA-mediated transfer of **metastatic** capability through two rounds of transfection into non-**metastatic** tumour cells and a **metastasis**-associated human DNA fragment has been recovered from the transfectants and sequenced. Using primers designed to anneal to a coding region identified by computer analysis within the novel sequence, it has been shown with RT-PCR that it is heavily expressed in **metastatic** **cancer** tissues, but not in corresponding normal ones. This could be of value in assessing the prognosis of patients using small biopsy samples from their primary tumours and the potential of this sequence for such purposes and for possible therapeutic intervention is currently being explored.

Recent work in several laboratories has shown that elevated expression of certain other specific growth factor genes, including c-met and **EGFR**, correlates with **metastatic** capability. Combined evaluation of such markers in further studies will in time give useful information on the prognosis of individual patients to guide therapeutic decisions and the implications of these recent advances for clinical practice and future research are discussed below. (C) 1993 Wiley-Liss, Inc.

L20 ANSWER 5 OF 6 MEDLINE
ACCESSION NUMBER: 90199802 MEDLINE
DOCUMENT NUMBER: 90199802 PubMed ID: 1690599
TITLE: Clinical implications of the expression of **epidermal growth factor** **receptors** in human transitional cell **carcinoma.**
AUTHOR: Messing E M
CORPORATE SOURCE: Department of Surgery and Human Oncology, University of Wisconsin School of Medicine, Madison 53792.
CONTRACT NUMBER: R01-CA44801 (NCI)
SOURCE: CANCER RESEARCH, **(1990 Apr 15)** 50 (8) 2530-7. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 20000303
Entered Medline: 19900503

AB To evaluate the distribution and density of epidermal growth factor (EGF) receptors (EGF-Rs) on urothelium, immunohistological studies using a monoclonal **antibody** to the binding portion of the human EGF-R were performed on frozen specimens of normal urothelium (N = 20), urothelium from patients with nonurothelial urological malignancies (N = 15) and inflammatory diseases (N = 8), low grade superficial transitional cell **carcinomas** (TCC) (N = 13), high grade superficial or invasive TCC (N = 28), and endoscopically normal appearing urothelium from patients with low grade superficial (N = 5) or high grade (N = 21) TCC elsewhere in the **bladder** (or ipsilateral renal pelvis/ureter). EGF-Rs are found only on the basal layer of epithelial cells (with scattered representation on intermediate cells) in 95% of normal urothelial specimens and 100% of pathological specimens without urothelial malignancy. Alternatively, 92.3% of specimens of low grade superficial TCC and 100% of high grade TCCs had EGF-Rs richly expressed on the superficial as well as the deeper layers of urothelium. This "malignant" distribution of EGF-Rs was also found on all specimens of endoscopically normal appearing urothelium in patients with TCC elsewhere. The density of EGF-Rs correlated closely with **tumor** grade on both "premalignant" and frankly **neoplastic** urothelium. We conclude that the expression of EGF-Rs on urothelium favors the interaction of

premalignant and malignant tissue with **urinary** EGF. To determine if altering the physiochemical environment of **urine** could interfere with this interaction, the effects of pH on the binding of and growth responses to EGF were assessed on four human TCC cell lines. Scatchard plots demonstrated that varying pH from 5.0 to 7.5 did not significantly change the total number of receptors, but EGF-R affinity was reduced approximately 20-fold as pH decreased from 7.5 to 5 in each TCC target. Similarly, significant growth stimulation by EGF at pH 7.5 was abrogated at pH less than or equal to 7.0 while growth rates in the absence of EGF remained unchanged at lower pHs. It thus appears that **urinary** acidification may hold promise in the management and prevention of recurrent **bladder cancer.**

L20 ANSWER 6 OF 6 MEDLINE
ACCESSION NUMBER: 90294381 MEDLINE
DOCUMENT NUMBER: 90294381 PubMed ID: 2359180
TITLE: A new 180 kDa. **urine** protein marker associated with **bladder cancer.**
AUTHOR: Zhau H Y; Babaian R J; Hong S J
CORPORATE SOURCE: Department of Urology, University of Texas M. D. Anderson Cancer Center, Houston 77030.
CONTRACT NUMBER: RR551-26 (NCRR)
SOURCE: JOURNAL OF UROLOGY, **(1990 Jul)** 144 (1) 47-52.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199007
ENTRY DATE: Entered STN: 19900907
Last Updated on STN: 20000303
Entered Medline: 19900731

AB We surveyed the **tumor**-related proteins present in the **urine** specimens of 118 **bladder cancer** patients to seek a possible marker enabling future diagnosis and prognosis of this disease. We identified a protein of 180 kDa. by sodium dodecyl sulfate polyacrylamide gel electrophoresis in **urine** samples subjected to prior adsorption by protein-A conjugated to a sepharose bead. This protein appears to be a glycoprotein because it binds to concanavalin A-conjugated sepharose and can be eluted by alpha-methyl D-mannoside. It does not react immunochemically with **antibodies** prepared against either carcinoembryonic antigen or **epidermal growth factor receptor**, both of which have an apparent molecular weight close to 180 kDa. We found this protein in the **urine** of 74.3% of the patients with transitional cell **carcinoma.** It was not present in age-matched controls, patients with benign prostatic hyperplasia or patients with 10 other **cancers.** There was 1 false positive result in a patient with prostate **cancer.** It does not appear to be associated with **urinary** tract infection, blood contamination, premedication or anesthesia.

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 NEWS 38  May 15  Supporter information for ENCOMPPAT and ENCOMPLIT updated
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 NEWS 40  May 19  Simultaneous left and right truncation added to WSCA
 NEWS 41  May 19  RAPRA enhanced with new search field, simultaneous left and
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 NEWS 42  Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43  Jun 06  PASCAL enhanced with additional data

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
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L2           7 DUP REM L1 (16 DUPLICATES REMOVED)

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L2   ANSWER 1 OF 7     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   1998365395     MEDLINE
DOCUMENT NUMBER:    98365395   PubMed ID: 9698374
TITLE:              Identification of the domains of photoincorporation of the
                    3'- and 7-benzophenone analogues of taxol in the
                    carboxyl-terminal half of murine mdr1b P-glycoprotein.
AUTHOR:             Wu Q; Bounaud P Y; Kuduk S D; Yang C P; Ojima I; Horwitz S
                    B; Orr G A
```

CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
CONTRACT NUMBER: CA39821 (NCI)
GM 42798 (NIGMS)
HD 27569 (NICHD)
+
SOURCE: BIOCHEMISTRY, (1998 Aug 11) 37 (32) 11272-9.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980910

AB P-glycoprotein is an ATP-dependent drug-efflux pump that can transport a diverse range of structurally and functionally unrelated hydrophobic compounds across the plasma membrane. The transporter is composed of two homologous halves, each containing a nucleotide binding fold and six putative transmembrane spanning segments. The contact domains between the murine mdr1b P-glycoprotein and two photoreactive Taxol analogues have been mapped by a combination of CNBr digestion and immunoprecipitation studies. We had demonstrated previously that the 3'-p-benzoyldihydrocinnamoyl (BzDC) analogue of Taxol specifically photolabeled mdr1b P-glycoprotein and now show that the corresponding C-7 analogue likewise specifically photoincorporates into the transporter. CNBr digestion of both photolabeled P-glycoproteins gave rise to an approximate 10 kDa tritium-labeled peptide, each of which was a distinct polypeptide. The CNBr fragment generated from the 3'-BzDC-Taxol-photolabeled P-glycoprotein was immunoprecipitated by a **polyclonal** antibody (Ab7) raised against amino acid residues 1008-1019 of the mdr1b isoform. In contrast, the CNBr fragment generated from the 7-BzDC-Taxol-photolabeled P-glycoprotein was immunoprecipitated by a **polyclonal** antibody (**Ab4**) raised against amino acid residues 740-750. The specificity of these reactions was demonstrated by showing that the presence of the appropriate synthetic peptide blocked the immunoprecipitation. Moreover when the antibodies were reversed, no immunoprecipitation occurred. Based on the deduced amino acid sequence of mdr1b P-glycoprotein, and its hydropathy plot analysis, our data indicated that the 3'-BzDC group photoincorporates into amino acid residues 985-1088, a region of the transporter that includes half of TM 12 and terminates just after the Walker A motif in the second nucleotide binding fold. The 7-BzDC group photoincorporates into amino acid residues 683-760, a region of the transporter that includes all of TM 7 and half of TM 8 plus the intervening extracellular loop.

L2 ANSWER 2 OF 7 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 94154977 MEDLINE
DOCUMENT NUMBER: 94154977 PubMed ID: 8111580
TITLE: Calcitonin elevation in small cell lung cancer without ectopic production.
AUTHOR: Kelley M J; Becker K L; Rushin J M; Venzon D; Phelps R; Ihde D C; Bliss D P Jr; Melby K; Snider R H; Johnson B E
CORPORATE SOURCE: NCI-Navy Medical Oncology Branch, National Cancer Institute, National Naval Medical Center, Bethesda, MD 20889-5105.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, (1994 Jan) 149 (1) 183-90.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199403

ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19970203
Entered Medline: 19940328

AB To determine the relative contribution of ectopic calcitonin (CT) production versus nonectopic secretion of CT in patients with small cell lung cancer (SCLC), serum and urine immunoreactive CT (iCT) levels of 86 different subjects were measured by radioimmunoassay (RIA) using two **polyclonal** antisera (Ab3b and **Ab4**). The subjects included 49 previously untreated patients with SCLC, 17 smokers, and 20 nonsmokers. Serum and urine iCT values were highest in the patients with SCLC, intermediate in the smokers, and lowest in the nonsmokers ($p < 0.0003$). Sixteen of the 49 patients with SCLC had tumor cell lines available for determination of CT mRNA expression by RNase protection assay (RPA) and iCT production by RIA. CT mRNA was detected in nine of 16 subjects and iCT in eight of 16. The tumor cell lines of seven patients had undetectable CT by both RPA and RIA, and of these, five had elevated urine or serum iCT values compared with those of nonsmokers, and two had levels above all values in the smoker group. Immunohistochemical staining of formalin-fixed, paraffin-embedded tumor samples detected iCT in two of four tumors from patients whose tumor cell lines had CT mRNA by RPA and iCT by RIA, but in none of six whose tumor cell lines had undetectable CT mRNA. Thus, increased iCT values in some patients with SCLC are likely due to sources other than CT production by tumor cells.

L2 ANSWER 3 OF 7 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92011895 MEDLINE
DOCUMENT NUMBER: 92011895 PubMed ID: 1655807
TITLE: Retinoic acid receptor gamma: specific immunodetection and phosphorylation.
AUTHOR: Rochette-Egly C; Lutz Y; Saunders M; Scheuer I; Gaub M P; Chambon P
CORPORATE SOURCE: Laboratoire de Genetique Moleculaire des Eucaryotes du Centre National pour la Recherche Scientifique, l'Institut National de la Sante et de la Recherche Medicale, Faculte de Medecine, Strasbourg, France.
SOURCE: JOURNAL OF CELL BIOLOGY, (1991 Oct) 115 (2) 535-45.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19970203
Entered Medline: 19911113

AB Synthetic peptides corresponding to cDNA-deduced amino acid sequences unique to the human and mouse retinoic acid receptor gamma 1 (hRAR-gamma 1 and mRAR-gamma 1, respectively) were used to generate anti-RAR-gamma 1 antibodies. Four mAbs were selected, which were directed against peptides found in region A1 (Ab1 gamma (A1)), region F (Ab2 gamma (mF) and **Ab4** gamma (hF)) and region D2 (Ab5 gamma (D2)). These antibodies specifically immunoprecipitated and recognized by Western blotting RAR-gamma 1 proteins in COS-1 cells transfected with expression vectors containing the RAR-gamma 1 cDNAs. They all reacted with both human and mouse RAR-gamma 1 proteins, except **Ab4** gamma (hF) that was specific for hRAR-gamma 1. Rabbit **polyclonal** antibodies, directed against a peptide from the mRAR-gamma 1 F region were also obtained (RP gamma (mF)) and found to be specific for mouse RAR-gamma 1 protein. Furthermore, in gel retardation/shift assays the antibodies specifically retarded the migration of complexes obtained with a RA response element (RARE). Antibodies raised against regions D2 and F also recognized the RAR-gamma 2 isoform which differs from RAR-gamma 1 only in the A region. On the other hand, antibodies directed against the A1 region of RAR-gamma 1 (Ab1 gamma (A1)) only reacted with the RAR-gamma 1 protein. The antibodies characterized here allowed us to detect the

presence of mRAR-gamma 1 and gamma 2 isoforms in mouse embryos and F9 embryonal carcinoma cells nuclear extracts. They were also used to demonstrate that the mRAR-gamma 1 protein can be phosphorylated and that the phosphorylation occurs mainly in the NH2-terminal A/B region.

L2 ANSWER 4 OF 7 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 91:579671 SCISEARCH
THE GENUINE ARTICLE: GL281
TITLE: RETINOIC ACID RECEPTOR-GAMMA - SPECIFIC IMMUNODETECTION AND PHOSPHORYLATION
AUTHOR: ROCHETTEEGLY C (Reprint); LUTZ Y; SAUNDERS M; SCHEUER I; GAUB M P; CHAMBON P
CORPORATE SOURCE: FAC MED STRASBOURG, INST CHIM BIOL, INSERM, UNITE BIOL MOLEC & GENIE GENET 184, CNRS, F-67085 STRASBOURG, FRANCE (Reprint)
COUNTRY OF AUTHOR: FRANCE
SOURCE: JOURNAL OF CELL BIOLOGY, (1991) Vol. 115, No. 2, pp. 535-545.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 48
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Synthetic peptides corresponding to cDNA-deduced amino acid sequences unique to the human and mouse retinoic acid receptor gamma-1 (hRAR-gamma-1 and mRAR-gamma-1, respectively) were used to generate anti-RAR-gamma-1 antibodies. Four mAbs were selected, which were directed against peptides found in region A1 (Ab1-gamma(A1)), region F (Ab2-gamma(mF) and **Ab4**-gamma(hF)) and region D2 (Ab5-gamma(D2)). These antibodies specifically immunoprecipitated and recognized by Western blotting RAR-gamma-1 proteins in COS-1 cells transfected with expression vectors containing the RAR-gamma-1 cDNAs. They all reacted with both human and mouse RAR-gamma-1 proteins, except **Ab4**-gamma(hF) that was specific for hRAR-gamma-1. Rabbit **polyclonal** antibodies, directed against a peptide from the mRAR-gamma-1 F region were also obtained (RP-gamma(mF)) and found to be specific for mouse RAR-gamma-1 protein. Furthermore, in gel retardation/shift assays the antibodies specifically retarded the migration of complexes obtained with a RA response element (RARE). Antibodies raised against regions D2 and F also recognized the RAR-gamma-2 isoform which differs from RAR-gamma-1 only in the A region. On the other hand, antibodies directed against the A1 region of RAR-gamma-1 (Ab1-gamma(A1)) only reacted with the RAR-gamma-1 protein. The antibodies characterized here allowed us to detect the presence of mRAR-gamma-1 and gamma-2 isoforms in mouse embryos and F9 embryonal carcinoma cells nuclear extracts. They were also used to demonstrate that the mRAR-gamma-1 protein can be phosphorylated and that the phosphorylation occurs mainly in the NH2-terminal A/B region.

L2 ANSWER 5 OF 7 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 90347197 MEDLINE
DOCUMENT NUMBER: 90347197 PubMed ID: 2384665
TITLE: Angiotensin II (AII)-related idiotypic network. III. Comparative analysis of idiotopes and paratopes borne by monoclonal antibodies raised against AII (AB1) and its internal image (AB3).
AUTHOR: Budisavljevic M; Ronco P M; Verroust P J
CORPORATE SOURCE: INSERM U.64 Hopital Tenon, Paris, France.
SOURCE: JOURNAL OF IMMUNOLOGY, (1990 Sep 1) 145 (5) 1440-9. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 19901026

Last Updated on STN: 19901026
Entered Medline: 19900920

AB We have previously produced mAb against angiotensin II (AII), a phylogenetically conserved vasopressive octapeptide, and shown that they identify four distinct epitopes on the AII molecule. In addition we used internal image bearing **polyclonal** antiidiotypic antibodies raised against rabbit anti AII to produce mAb3. In this study we analyze the segregation of the idiotypic and paratopic repertoires of the mAb1 and mAb3. Analysis of mAb1 carried out with **polyclonal** Ab2 raised against the four distinct paratopes permitted classification of the mAb1 into four categories: (p+, id+) comprises antibodies with shared paratopic and idiotypic specificities: (p+, id-) is made up of antibodies that fail to express the Id defined by Ab2 raised against other antibodies pertaining to the same paratopic group; (p-, id+) includes antibodies that express cross-reactive Id on distinct paratopes; (p-, id-) refers to antibodies unrelated by their paratopes and Id mAb2 confirmed these results and showed expression of identical or closely related Id on clearly distinct paratopes. At the Ab3 level, using **polyclonal** **Ab4**, there was a higher degree of Id cross-reactivity between the two paratopes available. These data suggest that the parallel set concept may apply to the immune response to a natural peptidic Ag and its internal image. Comparison of idiotypic repertoires of mAb1 and mAb3 (using Ab2 and **Ab4** antibodies) confirmed the lack of public Id and showed the predominance on mAb3 of "new" idiotypes absent from mAb1 molecules, as expected for internal image-induced antibodies. Cross-reactive idiotypes defined on mAb1 and conserved on mAb3 were expressed on the two paratopes defined at the Ab3 level. They were located on the H chain of the homologous paratope and required the association of H and L chains on the heterologous paratope. Our analysis suggests that, in the AII system, the idiotypic and paratopic repertoires segregate at least in part independently. The paratopic repertoire is limited to a small number of phylogenetically conserved specificities and may be encoded by germline genes. In contrast, the idiotypic repertoire is broader with respect to specificities, species, and localization on H and L chains. This extended diversity may be generated by somatic mutations or use of various combinations of H and L chains and/or V, D, J segments.

L2 ANSWER 6 OF 7 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 90371934 MEDLINE
DOCUMENT NUMBER: 90371934 PubMed ID: 2396474
TITLE: Protective effect of **polyclonal** and monoclonal antibodies against abortion in mice infected by Chlamydia psittaci.
AUTHOR: Buzoni-Gatel D; Bernard F; Andersen A; Rodolakis A
CORPORATE SOURCE: INRA, Station de Pathologie de la Reproduction, Nouzilly, France.
SOURCE: VACCINE, (1990 Aug) 8 (4) 342-6.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901109
Last Updated on STN: 19901109
Entered Medline: 19901011

AB The role of antibody in preventing placental and fetal infection by Chlamydia psittaci was studied in mice. Pregnant mice were passively immunized with **polyclonal** sera or monoclonal antibodies (mAbs) at day 11 of gestation. The mice were intravenously challenged the following day with the virulent AB7 ovine abortion strain of C. psittaci. Mice were either killed on day 16 of gestation to determine placental and fetal chlamydial infection levels or were permitted to have and raise their young until 8 days old for comparison of survival rates. Immune sera produced a decrease in both placental and fetal infection and reduced

the number of young dying in utero or shortly after birth. **Polyclonal** sera to the highly invasive AB7 and **AB4** strains or to the invasive 1B strain were more effective than serum to the invasive AB13 strain. The B577/F3 and B577/A11 monoclonal antibodies gave almost complete protection, with only low levels of placental infection and no detectable fetal infection or decrease in survival rate. The study demonstrates that immune sera and type-specific mAbs can passively transfer resistance to placental and fetal colonization and to abortion and fetal loss in mice intravenously challenged with P. psittaci.

L2 ANSWER 7 OF 7 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 88163650 MEDLINE
DOCUMENT NUMBER: 88163650 PubMed ID: 3126813
TITLE: Identification of a receptor binding region on the beta subunit of human follicle-stimulating hormone.
AUTHOR: Schneyer A L; Sluss P M; Huston J S; Ridge R J; Reichert L E Jr
CORPORATE SOURCE: Department of Biochemistry, Albany Medical College, New York 12208.
CONTRACT NUMBER: HD-07252 (NICHD)
HD-19302 (NICHD)
HD-21388 (NICHD)
SOURCE: BIOCHEMISTRY, (1988 Jan 26) 27 (2) 666-71.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198805
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880505

AB Mouse epidermal growth factor (mEGF) and the beta subunit of follicle-stimulating hormone (hFSH) (hFSH-beta) have been shown to inhibit binding of intact hFSH to its testes membrane receptor in vitro. Both hFSH-beta and mEGF contain the tetrapeptide sequence Thr-Arg-Asp-Leu (TRDL). Previous results demonstrated that synthetic TRDL inhibited binding of intact hFSH to receptor. We therefore investigated the possibility that TRDL was located on an exposed region of FSH-beta using a **polyclonal** antiserum to hFSH [NHPP anti-hFSH batch 4 (**AB4**)] which recognized determinants on intact hFSH and its beta subunit, but not the alpha subunit. Pituitary FSH preparations from several mammalian species produced parallel inhibition curves in a heterologous [**AB4** and 125I-labeled ovine FSH (125I-oFSH)] radioimmunoassay with relative potencies similar to those observed for the same preparations assayed by radioligand receptor assay. This antiserum also competitively inhibited 125I-FSH binding to receptor. Thus, **AB4** appeared to recognize antigenic determinants that are highly conserved and located at or near regions involved with hormone recognition of receptor for FSH. Synthetic TRDL inhibited 50% of 125I-hFSH binding to antiserum at a concentration of 1.36 mg/tube (9 x 10(-3) M). Other tetrapeptides (Thr-Pro-Arg-Lys and Lys-Thr-Cys-Thr) had no inhibitory activity at comparable concentrations. A mixture of the free amino acids T, R, D, and L inhibited radioligand binding only at significantly higher concentrations than TRDL. (ABSTRACT TRUNCATED AT 250 WORDS)

=> s EGFR and ab4
L3 0 EGFR AND AB4

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	10.57	10.78

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INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS,
      BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT,
      CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE,
      DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 16:43:19 ON 16 JUN 2003

67 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s egfr and ab4
  31 FILES SEARCHED...
  59 FILES SEARCHED...
         2   FILE USPATFULL
         1   FILE WPIDS
         1   FILE WPINDEX

   3 FILES HAVE ONE OR MORE ANSWERS,   67 FILES SEARCHED IN STNINDEX

L4   QUE EGFR AND AB4

=> file uspatfull wpids wpindex
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               3.85      14.63

FILE 'USPATFULL' ENTERED AT 16:47:29 ON 16 JUN 2003
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FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s egfr and ab4
L5            3 EGFR AND AB4

=> d ibib abs 1-3

L5   ANSWER 1 OF 3  USPATFULL
ACCESSION NUMBER:        2002:295147  USPATFULL
TITLE:                   Compositions and methods of treating tumors
INVENTOR(S):             Greene, Mark I., Penn Valley, PA, UNITED STATES
                         O'Rourke, Donald M., Wynnewood, PA, UNITED STATES
                         Murali, Ramachandran, Drexel Hill, PA, UNITED STATES
                         Park, Byeong-Woo, Wayne, PA, UNITED STATES

                              NUMBER       KIND    DATE
                         --------------- ------ --------
PATENT INFORMATION:      US 2002165193      A1   20021107
APPLICATION INFO.:       US 2002-100952     A1   20020319  (10)
RELATED APPLN. INFO.:    Continuation of Ser. No. US 1998-111681, filed on 8 Jul
                         1998, PENDING

                               NUMBER        DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 1998-76788P     19980304 (60)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR,
                         1650 MARKET STREET, PHILADELPHIA, PA, 19103
NUMBER OF CLAIMS:        25
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      6 Drawing Page(s)
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LINE COUNT: 4794
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treating an individual who has an erbB protein mediated tumor is disclosed. Methods of preventing erbB protein mediated tumors in an individual are disclosed. The methods comprise adminstering to the individual a nucleic acid molecule that encodes a protein that dimerizes with an erbB protein and that is deficient in tyrosine kinase activity. Composition that comprise such nucleic acid molecules including pharmaceutical compositions are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 3 USPATFULL
ACCESSION NUMBER: 2001:125533 USPATFULL
TITLE: In vitro and in vivo assay for agents which treat mucus hypersecretion
INVENTOR(S): Nadel, Jay A., San Francisco, CA, United States
Takeyama, Kiyoshi, San Francisco, CA, United States
PATENT ASSIGNEE(S): The University of California, San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6270747	B1	20010807	
APPLICATION INFO.:	US 1999-375597		19990817	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-97023P	19980818	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: LeGuyader, John L.
ASSISTANT EXAMINER: Zara, Jane
LEGAL REPRESENTATIVE: Borden, Paula A., Sherwood, PamelaBozicevic, Field & Francis
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 3
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 2604
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Hypersecretion of mucus in the lungs is inhibited by the administration of an epidermal growth factor receptor (EGF-R) antagonist. The EGF-R antagonist may be in the form of a small organic molecule, an antibody, or portion of an antibody that binds to and blocks the EGF receptor. The EGF-R antagonist is preferably administered by injection in an amount sufficient to inhibit formation of goblet cells in pulmonary airways. The degranulation of goblet cells that results in airway mucus production is thereby inhibited. Assays for screening candidate agents that inhibit goblet cell proliferation are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 3 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-303486 [26] WPIDS
DOC. NO. NON-CPI: N2000-226752
DOC. NO. CPI: C2000-092081
TITLE: A marker for bladder cancer, prostate cancer or urinary infection comprises a fragment of epidermal growth factor receptor.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MCKEOWN, S; RITCHIE, J
PATENT ASSIGNEE(S): (UYUL-N) UNIV ULSTER AT JORDANSTOWN
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000019208	A1	20000406	(200026)*	EN	18

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

AU 9961076	A	20000417	(200035)		
EP 1117998	A1	20010725	(200143)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000019208	A1	WO 1999-GB3235	19990930
AU 9961076	A	AU 1999-61076	19990930
EP 1117998	A1	EP 1999-947700	19990930
		WO 1999-GB3235	19990930

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9961076	A	Based on	WO 200019208
EP 1117998	A1	Based on	WO 200019208

PRIORITY APPLN. INFO: GB 1998-21170 19980930

AN 2000-303486 [26] WPIDS

AB WO 200019208 A UPAB: 20000531

NOVELTY - A marker for bladder cancer, prostate cancer or urinary infection, the marker comprises a 37 kDa fragment of epidermal growth factor receptor (**EGFR**).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for the diagnosis of first presentation or recurrence of bladder cancer, the method comprising the detection of a 37 kDa fragment of **EGFR** in a urine sample;

(2) the use of antibody **Ab4 EGFR** in a test to detect the presence of 37 kDa **EGFR** fragment in urine as a diagnostic test for bladder cancer;

(3) a method for the diagnosis of prostate cancer, the method comprising the detection of a 37 kDa fragment of **EGFR** in a urine sample;

(4) the use of antibody **Ab4 EGFR** in a test to detect the presence of 37 kDa **EGFR** fragment in urine as a diagnostic test for prostate cancer;

(5) a method for the diagnosis of bladder cancer, and/or prostate cancer and/or urinary infection, the method comprising a test for the presence of a 37 kDa fragment of **EGFR** in a urine sample; and

(6) the use of antibodies to the 37 kDa fragment of **EGFR** in the diagnosis of urinary infection, bladder cancer and prostate cancer.

USE - The methods are useful for the diagnosis of bladder cancer and detecting the recurrence of bladder or prostate cancer (claimed).

ADVANTAGE - The method is a simple dip stick test and provides a simple non-invasive urinary test which would allow for the detection of first presentation and recurrent bladder cancer.

Dwg.0/0

=>

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	73.44	88.07

STN INTERNATIONAL LOGOFF AT 17:03:51 ON 16 JUN 2003

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642GXN

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY